CATALYST

Supplementary Appendix 3 – Summary of CATALYST protocol changes

Amendment number	Date of approval	Protocol version number	Type of amendment	Summary of amendment
1	**REC:** 14-May-20	n/a	Substantial Amendment	Addition of Oxford and UCL as sites
2	**MHRA:** 29-May-20 **HRA:** 01-Jun-20	3.0	Substantial Amendment	Addition of two new IMPs: Namilumab and Infliximab. Update SOE, amendments to inclusion/ exclusion criteria. Specifically: New exclusion criteria relating to the addition of the new drugs: 1) Known hypersensitivity to drug products or excipients 2) Patients with tuberculosis or other severe infections such as (non-COVID-19) sepsis, abscesses, and opportunistic infections requiring treatment 3) Patients with moderate or severe heart failure (NYHA class III/IV)
3	**REC:** 10-Jun-20	n/a	Substantial Amendment	Addition of new sites
4	**MHRA:** 08-Jun-20	n/a	Substantial Amendment	IMPD update
5	**MHRA:** 12-Jun-20 **REC:** 12-Jun-20	4.0	Substantial Amendment	Amendment to inclusion criteria. Specifically: Inclusion criterion 1 changed to: 'Hospitalised adult (≥16 yrs) patients with a clinical picture strongly suggestive of SARS-CoV-2 pneumonia (confirmed by chest X-ray or CT scan, with or without a positive reverse transcription polymerase chain reaction [RT-PCR] assay)' in order to: • Allow CT imaging as evidence for COVID-19 pneumonia • Allow recruitment of patients with strong clinical suspicion for COVID-19 pneumonia but with negative PCR assay
6	**MHRA:** 19-Jun-20 **REC:** 20-Jun-20	5.0	Substantial Amendment	Non-substantial amendments to Sample Collection Sub-study text. Amendment to exclusion criteria. Specifically: 'Concurrent immunosuppression with biological agents or prednisone dose > 20mg' Was changed to 'Concurrent immunosuppression with biological agents' in order to allow patients to be recruited on dexamethasone, following the RECOVERY data

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7	**MHRA:** 12-Oct-20 **REC:** 12-Oct-20	6.0	Substantial Amendment	Change of Primary and Secondary Outcomes Specifically: Primary outcome changed to CRP (previously a secondary outcome) from the oxygen saturation to fractional inspired oxygen concentration (SpO2/FiO2) ratio, which now becomes a secondary outcome Hospital free days added as a secondary outcome Overall survival listed as a safety measure (previously death included under hospital survival status as a clinical outcome) Applicable changes to Inclusion/ Exclusion Criteria Specifically: Inclusion criteria changed from 'Oxygen saturation (SaO2) of ≤94% while breathing ambient air or a ratio of the partial pressure of Oxygen (PaO2) to the fraction of inspired oxygen (FiO2) (PaO2:FiO2) ≤ 300 mg Hg (≤40kPa'), to 'CRP ≥40' The following exclusion criteria that relate to the unopened Myelotarg arm were removed from general exclusion and made arm specific: • Known veno-occlusive disease • Neutrophil count < 2 x 109/l or White Blood Cell Count < 4.0 x 109/l The following exclusion criteria was removed as it was felt to be unnecessarily hindering recruitment: • Chronic Obstructive Pulmonary Disease (known FEV1 < 50% predicted or ambulatory or long term oxygen therapy Inclusion of Abbreviations list and eCRF table Update to Statistical Analysis section • Justification for CRP, operating characteristics and decision rules